

SEQUENCE LISTING

<110> Miao et al.

<120> METHOD OF TREATING DOPAMINERGIC AND GABA-NERGIC DISORDERS

<130> CIBT-P02-044

<140> 09/451939

<141> 1999-12-01

<150> 08/900220

<151> 1997-07-24

<160> 32

<170> PatentIn Ver. 2.1

<210> 1

<211> 1277

<212> DNA

<213> Gallus gallus

<400> 1

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<211> 1190

<212> DNA

<213> Mus musculus

<400> 2

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<210> 3

<211> 1281

<212> DNA

<213> Mus musculus

<400> 3

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<210> 4

<211> 1313

<212> DNA

<213> Mus musculus

<400> 4

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<210> 5

<211> 1256

<212> DNA

<213> Brachydanio rerio

<400> 5

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```

<210> 6

<211> 1425

<212> DNA

<213> Homo sapiens

<220>

<221> modified base

<222> (1387...1389)

<223> n=a, c, g, or t

<400> 6

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<210> 7

<211> 1622

<212> DNA

<213> Homo sapiens

<400> 7

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<210> 8

<211> 1190

<212> DNA

<213> Homo sapiens

<400> 8

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<210> 9

<211> 1251

<212> DNA

<213> Brachydanio rerio

<400> 9

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<210> 10

<211> 425

<212> PRT

<213> Gallus gallus

<400> 10

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```

Ile Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
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```

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg
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Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr
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Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly
      85             90             95

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```

Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu
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```

Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr
      115            120            125

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Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr
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Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys
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```

Tyr Gly Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
      165            170            175

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```

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
      180            185            190

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```

Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val
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```

His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly
      210            215            220

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Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp
 225 230 235 240
 Phe Leu Thr Phe Leu Asp Arg Met Asp Ser Ser Arg Lys Leu Phe Tyr
 245 250 255
 Val Ile Glu Thr Arg Gln Pro Arg Ala Arg Leu Leu Leu Thr Ala Ala
 260 265 270
 His Leu Leu Phe Val Ala Pro Gln His Asn Gln Ser Glu Ala Thr Gly
 275 280 285
 Ser Thr Ser Gly Gln Ala Leu Phe Ala Ser Asn Val Lys Pro Gly Gln
 290 295 300
 Arg Val Tyr Val Leu Gly Glu Gly Gly Gln Gln Leu Leu Pro Ala Ser
 305 310 315 320
 Val His Ser Val Ser Leu Arg Glu Glu Ala Ser Gly Ala Tyr Ala Pro
 325 330 335
 Leu Thr Ala Gln Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys
 340 345 350
 Tyr Ala Val Ile Glu Glu His Ser Trp Ala His Trp Ala Phe Ala Pro
 355 360 365
 Phe Arg Leu Ala Gln Gly Leu Leu Ala Ala Leu Cys Pro Asp Gly Ala
 370 375 380
 Ile Pro Thr Ala Ala Thr Thr Thr Thr Gly Ile His Trp Tyr Ser Arg
 385 390 395 400
 Leu Leu Tyr Arg Ile Gly Ser Trp Val Leu Asp Gly Asp Ala Leu His
 405 410 415
 Pro Leu Gly Met Val Ala Pro Ala Ser
 420 425
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 <211> 396
 <212> PRT
 <213> Mus musculus
 <400> 11
 Met Ala Leu Pro Ala Ser Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu
 1 5 10 15
 Ala Leu Ser Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
 20 25 30
 Arg Arg Tyr Val Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
 35 40 45
 Val Pro Ser Met Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
 50 55 60
 Gly Arg Val Thr Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn
 65 70 75 80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
 85 90 95
 Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile
 100 105 110
 Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
 115 120 125
 Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
 130 135 140
 Arg Ala Leu Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly
 145 150 155 160
 Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
 165 170 175
 Glu Ser Arg Asn His Ile His Val Ser Val Lys Ala Asp Asn Ser Leu
 180 185 190
 Ala Val Arg Ala Gly Gly Cys Phe Pro Gly Asn Ala Thr Val Arg Leu
 195 200 205
 Arg Ser Gly Glu Arg Lys Gly Leu Arg Glu Leu His Arg Gly Asp Trp
 210 215 220
 Val Leu Ala Ala Asp Ala Ala Gly Arg Val Val Pro Thr Pro Val Leu
 225 230 235 240
 Leu Phe Leu Asp Arg Asp Leu Gln Arg Arg Ala Ser Phe Val Ala Val
 245 250 255
 Glu Thr Glu Arg Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu
 260 265 270
 Val Phe Ala Ala Arg Gly Pro Ala Pro Ala Pro Gly Asp Phe Ala Pro
 275 280 285
 Val Phe Ala Arg Arg Leu Arg Ala Gly Asp Ser Val Leu Ala Pro Gly
 290 295 300
 Gly Asp Ala Leu Gln Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
 305 310 315 320
 Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
 325 330 335
 Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
 340 345 350
 Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
 355 360 365
 Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
 370 375 380
 Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Met Gly
 385 390 395

<210> 12
 <211> 411
 <212> PRT
 <213> Mus musculus

<400> 12

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Met Ser Pro Ala Trp Leu Arg Pro Arg Leu Arg Phe Cys Leu Phe Leu
 1           5           10           15

Leu Leu Leu Leu Leu Val Pro Ala Ala Arg Gly Cys Gly Pro Gly Arg
      20           25           30

Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
      35           40           45

Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
      50           55           60

Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
      65           70           75           80

Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
      85           90           95

Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
      100          105          110

Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
      115          120          125

Val Thr Glu Gly Arg Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
      130          135          140

His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
      145          150          155          160

Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
      165          170          175

Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
      180          185          190

Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
      195          200          205

Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala Leu Ser Ala Val Lys
      210          215          220

Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Thr Pro Thr Phe
      225          230          235          240

Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro Asn Arg Leu Arg Ala
      245          250          255

Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
      260          265          270

Pro Ala His Leu Leu Phe Ile Ala Asp Asn His Thr Glu Pro Ala Ala

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275 280 285
 His Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
 290 295 300
 Leu Val Ser Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
 305 310 315 320
 Ser Thr His Val Ala Leu Gly Ser Tyr Ala Pro Leu Thr Arg His Gly
 325 330 335
 Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
 340 345 350
 Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe Pro
 355 360 365
 Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu Gly Val His Ser Tyr
 370 375 380
 Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Ser Thr
 385 390 395 400
 Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
 405 410

<210> 13

<211> 437

<212> PRT

<213> Mus musculus

<400> 13

Met Leu Leu Leu Leu Ala Arg Cys Phe Leu Val Ile Leu Ala Ser Ser
 1 5 10 15
 Leu Leu Val Cys Pro Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly
 20 25 30
 Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe
 35 40 45
 Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu
 50 55 60
 Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn
 65 70 75 80
 Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp
 85 90 95
 Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile
 100 105 110
 Ser Val Met Asn Gln Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
 115 120 125
 Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly
 130 135 140
 Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly

145		150		155		160
Met Leu Ala Arg	Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr					
	165			170		175
Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val						
	180			185		190
Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu						
	195			200		205
Glu Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Arg Pro Gly Asp Arg						
	210			215		220
Val Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu						
	225			230		235
Thr Phe Leu Asp Arg Asp Glu Gly Ala Lys Lys Val Phe Tyr Val Ile						
	245			250		255
Glu Thr Leu Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu						
	260			265		270
Leu Phe Val Ala Pro His Asn Asp Ser Gly Pro Thr Pro Gly Pro Ser						
	275			280		285
Ala Leu Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val						
	290			295		300
Ala Glu Arg Gly Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser						
	305			310		315
Val Thr Leu Arg Glu Glu Glu Ala Gly Ala Tyr Ala Pro Leu Thr Ala						
	325			330		335
His Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val						
	340			345		350
Ile Glu Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu						
	355			360		365
Ala His Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Gly Gly						
	370			375		380
Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly						
	385			390		395
Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His						
	405			410		415
Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met						
	420			425		430
Ala Val Lys Ser Ser						
	435					

<210> 14

<211> 418

<212> PRT

<213> Brachydanio rerio

<400> 14

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Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser
 1           5           10           15

Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg
          20           25           30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
      35           40           45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
 50           55           60

Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65           70           75           80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
          85           90           95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser
          100           105           110

Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
      115           120           125

Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg
      130           135           140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr
      145           150           155           160

Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
          165           170           175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
      180           185           190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln
      195           200           205

Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val
      210           215           220

Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met
      225           230           235           240

Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu
          245           250           255

Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu
      260           265           270

Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala
      275           280           285

Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp
      290           295           300

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Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu
 305 310 315 320
 Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val
 325 330 335
 Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu
 340 345 350
 Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser
 355 360 365
 Phe Leu Ser Pro Lys Thr Pro Ala Val Gly Pro Met Arg Leu Tyr Asn
 370 375 380
 Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr
 385 390 395 400
 Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn
 405 410 415
 Ser Ser
 <210> 15
 <211> 475
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SITE
 <222> (463)
 <223> Xaa=unknown amino acid residue
 <400> 15
 Met Leu Leu Leu Ala Arg Cys Leu Leu Leu Val Leu Val Ser Ser Leu
 1 5 10 15
 Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys
 20 25 30
 Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
 35 40 45
 Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
 50 55 60
 Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65 70 75 80
 Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
 85 90 95
 Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser
 100 105 110
 Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
 115 120 125
 Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg

130					135					140					
Ala 145	Val	Asp	Ile	Thr	Thr 150	Ser	Asp	Arg	Asp	Arg 155	Ser	Lys	Tyr	Gly	Met 160
Leu	Ala	Arg	Leu	Ala 165	Val	Glu	Ala	Gly	Phe 170	Asp	Trp	Val	Tyr	Tyr 175	Glu
Ser	Lys	Ala	His 180	Ile	His	Cys	Ser	Val 185	Lys	Ala	Glu	Asn	Ser 190	Val	Ala
Ala	Lys	Ser 195	Gly	Gly	Cys	Phe	Pro 200	Gly	Ser	Ala	Thr	Val 205	His	Leu	Glu
Gln	Gly 210	Gly	Thr	Lys	Leu	Val 215	Lys	Asp	Leu	Ser	Pro 220	Gly	Asp	Arg	Val
Leu 225	Ala	Ala	Asp	Asp	Gln 230	Gly	Arg	Leu	Leu	Tyr 235	Ser	Asp	Phe	Leu	Thr 240
Phe	Leu	Asp	Arg	Asp 245	Asp	Gly	Ala	Lys	Lys 250	Val	Phe	Tyr	Val	Ile 255	Glu
Thr	Arg	Glu	Pro 260	Arg	Glu	Arg	Leu	Leu 265	Leu	Thr	Ala	Ala	His 270	Leu	Leu
Phe	Val	Ala 275	Pro	His	Asn	Asp	Ser 280	Ala	Thr	Gly	Glu	Pro 285	Glu	Ala	Ser
Ser	Gly 290	Ser	Gly	Pro	Pro	Ser 295	Gly	Gly	Ala	Leu	Gly 300	Pro	Arg	Ala	Leu
Phe 305	Ala	Ser	Arg	Val	Arg 310	Pro	Gly	Gln	Arg	Val 315	Tyr	Val	Val	Ala	Glu 320
Arg	Asp	Gly	Asp	Arg 325	Arg	Leu	Leu	Pro	Ala 330	Ala	Val	His	Ser	Val 335	Thr
Leu	Ser	Glu	Glu 340	Ala	Ala	Gly	Ala	Tyr 345	Ala	Pro	Leu	Thr	Ala 350	Gln	Gly
Thr	Ile	Leu 355	Ile	Asn	Arg	Val	Leu 360	Ala	Ser	Cys	Tyr	Ala 365	Val	Ile	Glu
Glu	His 370	Ser	Trp	Ala	His	Arg 375	Ala	Phe	Ala	Pro	Phe 380	Arg	Leu	Ala	His
Ala 385	Leu	Leu	Ala	Ala	Leu 390	Ala	Pro	Ala	Arg	Thr 395	Asp	Arg	Gly	Gly	Asp 400
Ser	Gly	Gly	Gly	Asp 405	Arg	Gly	Gly	Gly	Gly 410	Gly	Arg	Val	Ala	Leu	Thr
Ala	Pro	Gly	Ala 420	Ala	Asp	Ala	Pro	Gly 425	Ala	Gly	Ala	Thr	Ala 430	Gly	Ile
His	Trp	Tyr 435	Ser	Gln	Leu	Leu	Tyr 440	Gln	Ile	Gly	Thr	Trp	Leu	Leu	Asp
Ser	Glu	Ala	Leu	His	Pro	Leu	Gly	Met	Ala	Val	Lys	Ser	Ser	Xaa	Ser

450

455

460

Arg Gly Ala Gly Gly Gly Ala Arg Glu Gly Ala
465 470 475

<210> 16

<211> 411

<212> PRT

<213> Homo sapiens

<400> 16

Met Ser Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu
1 5 10 15

Leu Leu Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg
20 25 30

Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
35 40 45

Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
50 55 60

Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
65 70 75 80

Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
85 90 95

Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
100 105 110

Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
115 120 125

Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
130 135 140

His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
145 150 155 160

Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
165 170 175

Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
180 185 190

Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
195 200 205

Gln Val Arg Leu Glu Ser Gly Ala Arg Val Ala Leu Ser Ala Val Arg
210 215 220

Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe
225 230 235 240

Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro His Arg Leu Arg Ala
245 250 255

Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
260 265 270

Pro Ala His Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala
275 280 285

Arg Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
290 295 300

Leu Val Ala Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
305 310 315 320

Ser Thr His Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly
325 330 335

Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
340 345 350

Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His
355 360 365

Ser Leu Ala Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr
370 375 380

Pro Gln Leu Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser
385 390 395 400

Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
405 410

<210> 17

<211> 396

<212> PRT

<213> Homo sapiens

<400> 17

Met Ala Leu Leu Thr Asn Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu
1 5 10 15

Ala Leu Pro Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
20 25 30

Arg Arg Tyr Ala Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
35 40 45

Val Pro Gly Val Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
50 55 60

Gly Arg Val Ala Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn
65 70 75 80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
85 90 95

Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile
 100 105 110

Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
 115 120 125

Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
 130 135 140

Arg Ala Leu Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly
 145 150 155 160

Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
 165 170 175

Glu Ser Arg Asn His Val His Val Ser Val Lys Ala Asp Asn Ser Leu
 180 185 190

Ala Val Arg Ala Gly Gly Cys Phe Pro Gly Asn Ala Thr Val Arg Leu
 195 200 205

Trp Ser Gly Glu Arg Lys Gly Leu Arg Glu Leu His Arg Gly Asp Trp
 210 215 220

Val Leu Ala Ala Asp Ala Ser Gly Arg Val Val Pro Thr Pro Val Leu
 225 230 235 240

Leu Phe Leu Asp Arg Asp Leu Gln Arg Arg Ala Ser Phe Val Ala Val
 245 250 255

Glu Thr Glu Trp Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu
 260 265 270

Val Phe Ala Ala Arg Gly Pro Ala Pro Ala Pro Gly Asp Phe Ala Pro
 275 280 285

Val Phe Ala Arg Arg Leu Arg Ala Gly Asp Ser Val Leu Ala Pro Gly
 290 295 300

Gly Asp Ala Leu Arg Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
 305 310 315 320

Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
 325 330 335

Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
 340 345 350

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
 355 360 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
 370 375 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Leu Gly
 385 390 395

<210> 18

<211> 416

<212> PRT

<213> Brachydanio rerio

<400> 18

Met Asp Val Arg Leu His Leu Lys Gln Phe Ala Leu Leu Cys Phe Ile
 1 5 10 15

Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly
 20 25 30

Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
 35 40 45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys
 50 55 60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile
 65 70 75 80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn
 85 90 95

Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu
 100 105 110

Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr
 115 120 125

Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr
 130 135 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys
 145 150 155 160

Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
 165 170 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
 180 185 190

Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val

195	200	205
Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly 210	215	220
Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp 225	230	235 240
Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile 245	250	255
Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala 260	265	270
His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala 275	280	285
Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu 290	295	300
Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr 305	310	315 320
Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile 325	330	335
Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His 340	345	350
Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu 355	360	365
Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu 370	375	380
Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp 385	390	395 400
Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser 405	410	415

<210> 19

<211> 1416

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS.

<222> (1)..(1413)

<400> 19

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Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr	
1 5 10 15	

tgt ctc tcc ctg gga tgc caa atg cca cag ttc cag ttc cag ttc cag	96
Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln	
20 25 30	

ctc	caa	atc	cgc	agc	gag	ctc	cat	ctc	cgc	aag	ccc	gca	aga	aga	acg	144
Leu	Gln	Ile	Arg	Ser	Glu	Leu	His	Leu	Arg	Lys	Pro	Ala	Arg	Arg	Thr	
	35						40					45				
caa	acg	atg	cgc	cac	att	gcg	cat	acg	cag	cgt	tgc	ctc	agc	agg	ctg	192
Gln	Thr	Met	Arg	His	Ile	Ala	His	Thr	Gln	Arg	Cys	Leu	Ser	Arg	Leu	
	50					55					60					
acc	tct	ctg	gtg	gcc	ctg	ctg	ctg	atc	gtc	ttg	ccg	atg	gtc	ttt	agc	240
Thr	Ser	Leu	Val	Ala	Leu	Leu	Leu	Ile	Val	Leu	Pro	Met	Val	Phe	Ser	
	65				70				75						80	
ccg	gct	cac	agc	tgc	ggt	cct	ggc	cga	gga	ttg	ggt	cgt	cat	agg	gcg	288
Pro	Ala	His	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Leu	Gly	Arg	His	Arg	Ala	
			85					90						95		
cgc	aac	ctg	tat	ccg	ctg	gtc	ctc	aag	cag	aca	att	ccc	aat	cta	tcc	336
Arg	Asn	Leu	Tyr	Pro	Leu	Val	Leu	Lys	Gln	Thr	Ile	Pro	Asn	Leu	Ser	
	100							105					110			
gag	tac	acg	aac	agc	gcc	tcc	gga	cct	ctg	gag	ggt	gtg	atc	cgt	cgg	384
Glu	Tyr	Thr	Asn	Ser	Ala	Ser	Gly	Pro	Leu	Glu	Gly	Val	Ile	Arg	Arg	
	115						120					125				
gat	tcg	ccc	aaa	ttc	aag	gac	ctc	gtg	ccc	aac	tac	aac	agg	gac	atc	432
Asp	Ser	Pro	Lys	Phe	Lys	Asp	Leu	Val	Pro	Asn	Tyr	Asn	Arg	Asp	Ile	
	130					135					140					
ctt	ttc	cgt	gac	gag	gaa	ggc	acc	gga	gcg	gat	ggc	ttg	atg	agc	aag	480
Leu	Phe	Arg	Asp	Glu	Glu	Gly	Thr	Gly	Ala	Asp	Gly	Leu	Met	Ser	Lys	
	145				150				155						160	
cgc	tgc	aag	gag	aag	cta	aac	gtg	ctg	gcc	tac	tcg	gtg	atg	aac	gaa	528
Arg	Cys	Lys	Glu	Lys	Leu	Asn	Val	Leu	Ala	Tyr	Ser	Val	Met	Asn	Glu	
				165					170					175		
tgg	ccc	ggc	atc	cgg	ctg	ctg	gtc	acc	gag	agc	tgg	gac	gag	gac	tac	576
Trp	Pro	Gly	Ile	Arg	Leu	Leu	Val	Thr	Glu	Ser	Trp	Asp	Glu	Asp	Tyr	
			180					185					190			
cat	cac	ggc	cag	gag	tcg	ctc	cac	tac	gag	ggc	cga	gcg	gtg	acc	att	624
His	His	Gly	Gln	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	Ala	Val	Thr	Ile	
		195				200					205					
gcc	acc	tcc	gat	cgc	gac	cag	tcc	aaa	tac	ggc	atg	ctc	gct	cgc	ctg	672
Ala	Thr	Ser	Asp	Arg	Asp	Gln	Ser	Lys	Tyr	Gly	Met	Leu	Ala	Arg	Leu	
	210					215					220					
gcc	gtc	gag	gct	gga	ttc	gat	tgg	gtc	tcc	tac	gtc	agc	agg	cgc	cac	720
Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Ser	Tyr	Val	Ser	Arg	Arg	His	
	225				230				235						240	
atc	tac	tgc	tcc	gtc	aag	tca	gat	tcg	tcg	atc	agt	tcc	cac	gtg	cac	768
Ile	Tyr	Cys	Ser	Val	Lys	Ser	Asp	Ser	Ser	Ile	Ser	Ser	His	Val	His	
				245				250					255			
ggc	tgc	ttc	acg	ccg	gag	agc	aca	gcg	ctg	ctg	gag	agt	gga	gtc	cgg	816
Gly	Cys	Phe	Thr	Pro	Glu	Ser	Thr	Ala	Leu	Leu	Glu	Ser	Gly	Val	Arg	
			260					265					270			

aag ccg ctc ggc gag ctc tct atc gga gat cgt gtt ttg agc atg acc	864
Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr	
275 280 285	
gcc aac gga cag gcc gtc tac agc gaa gtg atc ctc ttc atg gac cgc	912
Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg	
290 295 300	
aac ctc gag cag atg caa aac ttt gtg cag ctg cac acg gac ggt gga	960
Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly	
305 310 315 320	
gca gtg ctc acg gtg acg ccg gct cac ctg gtt agc gtt tgg cag ccg	1008
Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro	
325 330 335	
gag agc cag aag ctc acg ttt gtg ttt gcg cat cgc atc gag gag aag	1056
Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys	
340 345 350	
aac cag gtg ctc gta cgg gat gtg gag acg ggc gag ctg agg ccc cag	1104
Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln	
355 360 365	
cga gtg gtc aag ttg ggc agt gtg cgc agt aag ggc gtg gtc gcg ccg	1152
Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro	
370 375 380	
ctg acc cgc gag ggc acc att gtg gtc aac tcg gtg gcc gcc agt tgc	1200
Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys	
385 390 395 400	
tat gcg gtg atc aac agt cag tcg ctg gcc cac tgg gga ctg gct ccc	1248
Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro	
405 410 415	
atg cgc ctg ctg tcc acg ctg gag gcg tgg ctg ccc gcc aag gag cag	1296
Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln	
420 425 430	
ttg cac agt tcg ccg aag gtg gtg agc tcg gcg cag cag cag aat ggc	1344
Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly	
435 440 445	
atc cat tgg tat gcc aat gcg ctc tac aag gtc aag gac tac gtg ctg	1392
Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu	
450 455 460	
ccg cag agc tgg cgc cac gat tga	1416
Pro Gln Ser Trp Arg His Asp	
465 470	

<210> 20

<211> 471

<212> PRT

<213> Drosophila melanogaster

<400> 20

Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr

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20	Gly	Cys	Gln
	Met	Pro	Gln
	25	Phe	Gln
		30	Phe
			Gln
Leu	Gln	Ile	Arg
35	Ser	Glu	Leu
	40	His	Leu
		45	Arg
			Arg
			Thr
Gln	Thr	Met	Arg
50	His	Ile	Ala
	55	His	Thr
		60	Gln
			Arg
			Cys
			Leu
			Ser
			Arg
			Leu
Thr	Ser	Leu	Val
65	Ala	Leu	Leu
	70	Ile	Val
		75	Leu
			Pro
			Met
			Val
			Phe
			Ser
Pro	Ala	His	Ser
	85	Cys	Gly
		Pro	Gly
		Arg	Gly
		90	Leu
			Gly
			Arg
			His
			Arg
			Ala
Arg	Asn	Leu	Tyr
100	Pro	Leu	Val
	105	Leu	Lys
		Gln	Thr
		Ile	Pro
		110	Asn
			Leu
			Ser
Glu	Tyr	Thr	Asn
115	Ser	Ala	Ser
	120	Gly	Pro
		Leu	Glu
		Gly	Val
		125	Ile
			Arg
			Arg
Asp	Ser	Pro	Lys
130	Phe	Lys	Asp
	135	Leu	Val
		Pro	Asn
		Tyr	Asn
		140	Arg
			Asp
			Ile
Leu	Phe	Arg	Asp
145	Glu	Glu	Gly
	150	Thr	Gly
		Ala	Asp
		155	Gly
			Leu
			Met
			Ser
			Lys
Arg	Cys	Lys	Glu
	165	Lys	Leu
		Asn	Val
		Leu	Ala
		170	Tyr
			Ser
			Val
			Met
			Asn
			Glu
			175
Trp	Pro	Gly	Ile
180	Arg	Leu	Leu
	185	Val	Thr
		Glu	Ser
		Trp	Asp
		190	Glu
			Asp
			Tyr
His	His	Gly	Gln
195	Glu	Ser	Leu
	200	His	Tyr
		Glu	Gly
		Arg	Ala
		205	Val
			Thr
			Ile
Ala	Thr	Ser	Asp
210	Arg	Asp	Gln
	215	Ser	Lys
		Tyr	Gly
		Met	Leu
		220	Ala
			Arg
			Leu
Ala	Val	Glu	Ala
225	Gly	Phe	Asp
	230	Trp	Val
		Ser	Tyr
		235	Val
			Ser
			Arg
			Arg
			His
Ile	Tyr	Cys	Ser
245	Val	Lys	Ser
	250	Asp	Ser
		Ser	Ile
		Ser	Ser
		His	Val
		255	His
Gly	Cys	Phe	Thr
260	Pro	Glu	Ser
	265	Thr	Ala
		Leu	Leu
		Glu	Ser
		270	Gly
			Val
			Arg
Lys	Pro	Leu	Gly
275	Glu	Leu	Ser
	280	Ile	Gly
		Asp	Arg
		Val	Leu
		285	Ser
			Met
			Thr
Ala	Asn	Gly	Gln
290	Ala	Val	Tyr
	295	Ser	Glu
		Val	Ile
		300	Leu
			Phe
			Met
			Asp
			Arg
Asn	Leu	Glu	Gln
305	Met	Gln	Asn
	310	Phe	Val
		Gln	Leu
		315	His
			Thr
			Asp
			Gly
			Gly
			320

Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro
325 330 335

Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys
340 345 350

Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln
355 360 365

Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro
370 375 380

Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys
385 390 395 400

Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro
405 410 415

Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln
420 425 430

Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly
435 440 445

Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu
450 455 460

Pro Gln Ser Trp Arg His Asp
465 470

<210> 21

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Degenerate Shh
polypeptide general formula

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Phe, Tyr, or Trp

<220>

<221> SITE

<222> (9)

<223> Xaa=Arg, His or Lys

<220>

<221> SITE

<222> (44)

<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser. or Thr

<220>

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<222> (85)

<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>
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<222> (93)
<223> Xaa=Lys, Arg, His, Asn, or Gln

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<221> SITE
<222> (98)
<223> Xaa=Lys, Arg or His

<220>
<221> SITE
<222> (112)
<223> Xaa=Ser, Thr, Tyr, Trp, or Phe

<220>
<221> SITE
<222> (132)
<223> Xaa=Lys, Arg or His

<220>
<221> SITE
<222> (137)
<223> Xaa=Met, Cys, Ser, or Thr

<220>
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<222> (139)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

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<222> (181)
<223> Xaa=Leu, Val, Met, Thr, or Ser

<220>
<221> SITE
<222> (183)
<223> Xaa=His, Phe, Tyr, Ser, Thr, Met, or Cys

<220>
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<222> (185)
<223> Xaa=Gln, Asn, Glu, or Asp

<220>
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<222> (186)
<223> Xaa=His, Phe, Tyr, Thr, Gln, Asn, Glu, or Asp

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<221> SITE
<222> (189)
<223> Xaa=Gln, Asn, Glu, Asp, Thr, Ser, Met, or Cys

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<222> (191)
<223> Xaa=Ala, Gly, Cys, Leu, Val, or Met

<220>
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 <222> (196)
 <223> Xaa=Arg, Lys, Met, Ile, Asn, Asp, Glu, Gln, Ser,
 Thr, or Cys

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 <223> Xaa=Arg, Lys, Met, or Ile

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 <222> (206)
 <223> Xaa=Ala, Gly, Cys, Asp, Glu, Gln, Asn, Ser, Thr,
 or Met

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 <222> (207)
 <223> Xaa=Ala, Gly, Cys, Asp, Asn, Glu, or Gln

<220>
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 <222> (209)
 <223> Xaa=Arg, Lys, Met, Ile, Asn, Asp, or Glu

<220>
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 <222> (211)
 <223> Xaa=Leu, Val, Met, or Ile

<220>
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 <222> (212)
 <223> Xaa=Phe, Tyr, Thr, His, or Trp

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 <222> (216)
 <223> Xaa=Ile, Val, Leu, or Met

<220>
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 <222> (217)
 <223> Xaa=Met, Cys, Ile, Leu, Val, Thr, or Ser

<220>
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 <222> (219)
 <223> Xaa=Leu, Val, Met, Thr, or Ser

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Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
 20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Xaa Arg Asn Ser Glu

35

40

45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
65 70 75 80

Asp Lys Leu Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp Pro Gly
85 90 95

Val Xaa Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Xaa
100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
115 120 125

Asp Arg Asp Xaa Ser Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala Val Glu
130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
145 150 155 160

Ser Val Lys Ala Glu Asn Ser Val Ala Ala Lys Ser Gly Gly Cys Phe
165 170 175

Pro Gly Ser Ala Xaa Val Xaa Leu Xaa Xaa Gly Gly Xaa Lys Xaa Val
180 185 190

Lys Asp Leu Xaa Pro Gly Asp Xaa Val Leu Ala Ala Asp Xaa Xaa Gly
195 200 205

Xaa Leu Xaa Xaa Ser Asp Phe Xaa Xaa Phe Xaa Asp Arg
210 215 220

<210> 22

<211> 167

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Degenerate
hedgehog polypeptide general formula

<220>

<221> SITE

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Pro, Phe, or Tyr

<220>

<221> SITE

<222> (8)

<223> Xaa=Gly, Ala, Val, Leu, or Ile

<220>

<221> SITE

<222> (9)

<223> Xaa=Gly, Ala, Val, Leu, Ile, Lys, His, or Arg

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<222> (12)
<223> Xaa=Lys, Arg or His

<220>
<221> SITE
<222> (13)
<223> Xaa=Phe, Trp or Tyr or an amino acid gap

<220>
<221> SITE
<222> (14)
<223> Xaa=Gly, Ala, Val, Leu, or Ile or an amino acid gap

<220>
<221> SITE
<222> (17)
<223> Xaa=Asn, Gln, His, Arg, or Lys

<220>
<221> SITE
<222> (19)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

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<222> (27)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

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<222> (29)
<223> Xaa=Ser, Thr, Gln, or Asn

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<222> (30)
<223> Xaa=Met, Cys, Gly, Ala, Val, Leu, Ile, Ser, or Thr

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<223> Xaa=Gly, Ala, Val, Leu, Ile, or Pro

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<222> (33)
<223> Xaa=Arg, His or Lys

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Pro Arg, His, or Lys

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<222> (41)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Phe, or Tyr

<220>
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<222> (44)
<223> Xaa=Arg, His or Lys

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

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<222> (46)
<223> Xaa=Thr or Ser

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<222> (48)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Asn, or Gln

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<222> (53)
<223> Xaa=Arg, His or Lys

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<222> (54)
<223> Xaa=Asp or Glu

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<222> (71)
<223> Xaa=Ser or Thr

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<222> (79)
<223> Xaa=Glu, Asp, Gln, or Asn

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<222> (83)
<223> Xaa=Glu or Asp

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<223> Xaa=Arg, His or Lys

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<223> Xaa=Gly, Ala, Val, Leu, or Ile

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<223> Xaa=Arg, His or Lys

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<222> (107)
<223> Xaa=Trp, Phe, Tyr, Arg, His, or Lys

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<222> (114)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, Thr, Tyr, or Phe

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<222> (115)
<223> Xaa=Gln, Asn, Asp, or Glu

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<223> Xaa=Asn, Gln, Thr, or Ser

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Thr, or Ser

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<220>
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Xaa Leu Xaa Pro Leu Xaa Tyr Lys Gln Phe Xaa Pro Xaa Xaa Xaa Glu
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Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa
 35 40 45

Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile
 50 55 60

Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg
 65 70 75 80

Cys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp
 85 90 95

Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His
 100 105 110

His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr
 115 120 125

Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala
 130 135 140

Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Xaa Xaa His Xaa

145

150

155

160

His Xaa Ser Val Lys Xaa Xaa
165

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<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

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aaatcgatgc gcgc

74

<210> 24

<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 24

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cgggatccgc gcgc

74

<210> 25

<211> 996

<212> DNA

<213> Homo sapiens

<400> 25

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ggttcgaatc cttccccac caccatcact ttcaaaagtc cgaagaatc tgctccctgc 120

ttgtgtgttg gaggtcgctg agtagtgccg gagtaaaatt taagctacaa caaggcaagg 180

cttgaccgac aattgcatga agaattctgct tagggttagg cgttttgccg tgcttcgcga 240

tgtacgggcc agatatacgc gttgacattg attattgact agttattaat agtaatcaat 300

tacggggcca ttagttcata gccatatat ggagttccgc gttacataac ttacggtaaa 360

tggcccgccg ggctgaccgc ccaacgaccc ccgcccattg acgtcaataa tgacgtatgt 420

tcccatagta acgccaatag ggactttcca ttgacgtcaa tgggtggact atttacggta 480

aactgcccac ttggcagtag atcaagtgtg tcatatgccg agtacgcccc ctattgacgt 540

caatgacggg aaatggcccg cctggcatta tgcccagtag atgaccttat gggactttcc 600

tacttggcag tacatctacg tattagtcac cgctattacc atggtgatgc ggttttggca 660

gtacatcaat gggcgtggat agcggtttga ctcacgggga tttccaagtc tccaccccat 720
 tgacgtcaat gggagtttgt tttggcacca aaatcaacgg gactttccaa aatgtcgtaa 780
 caactccgcc ccattgacgc aaatggggcg taggcgtgta cgggtgggagg tctatataag 840
 cagagctctc tggctaacta gagaaccac tgcttactgg cttatcgaaa ttaatacgac 900
 tcactatagg gagacccaag cttggtaccg agctcggatc gatctgggaa agcgcaagag 960
 agagcgaca cgcacacacc cgccgcgcgc actcgg 996

<210> 26
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> anti-sense construct

<400> 26
 gtcctggcgc cgccgccgcc gtcgcc 26

<210> 27
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<220>
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<400> 27
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<210> 28
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<220>
 <223> anti-sense construct

<400> 28
 gtgcacggaa aggtgcaggc cacact 26

<210> 29
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 <212> DNA
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<220>
 <223> primer

<400> 29
 ggctccggta tgtgc 15

<210> 30
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<212> DNA
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<220>
<223> primer

<400> 30
ggctccgcta tgtgc

15

<210> 31
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<220>
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<400> 31
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25

<210> 32
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<220>
<223> primer

<400> 32
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25

35